

REMARKS/ARGUMENTS

Claim 1-22 are pending in this application and are subject to a Restriction Requirement. Claims 2-8, 1, and 9-19 are examined to the extent that R₃ reads on piperidene. Claims 1 and 20 are rejected. Claims 2-19, 21 and 22 are objected to as being dependent upon a rejected base claim, but would be allowable upon deletion of the nonelected subject matter and rewritten in independent form including all limitations of the base claim and any intervening claims. Claims 4 and 5 are hereby canceled without prejudice or disclaimer as drawn to non-elected subject matter. Applicants respectfully reserve the right to pursue these claims in a divisional application. Claims 1 and 20 are hereby amended to remove non-elected species. Claim 2 is hereby rewritten in independent form including all limitations of the base claim and without including any non-elected species. Support for the amendment to claim 2 may be found in original claims 1 and 2. Claim 21 is hereby rewritten in independent form including all limitations of the base claim and without including any non-elected species. New claim 24 is hereby added. Support for claim 24 may be found in original claim 2. Applicants respectfully reserve the right to pursue all non-elected species in a divisional application. In view of the amendments and remarks made herein, Applicants respectfully request reconsideration of claims 1-3, 6-22 and 24.

Objections

Claims 2-19, 21 and 22 are objected to as being dependent upon a rejected base claim. Claim 2 has been rewritten in independent form, including all limitations from the base claim and deleting all non-elected species. Applicants submit that independent claim 2, and claims 3, 6-8, and 24, dependent thereon, are now in condition for allowance. Claim 21 has been rewritten in independent form, including all limitations from the base claim and deleting all non-elected species. Applicants submit that claims 21 and 22 are now in condition for allowance. Method claims 9-19 were previously rejected under 35 U.S.C. § 102(f). The rejection was dropped in view of the Rule 1.132 Declaration filed by Dr. Brueggemeier. Applicants submit that claims 9-19 are in condition for allowance.

Rejections under 35 U.S.C. § 103(a)

Claim 1 is rejected under 35 U.S.C. § 103(a) as unpatentable over Chiesi *et al.* (WO 98/29403, hereinafter referred to as “Chiesi”) in view of King *et al.* Medicinal Chemistry, pp. 206-209 (hereinafter referred to as “King”). Specifically, the Examiner asserts that one skilled in the art would be motivated to use SO or SO₂ in place of the CO in the compounds of Chiesi based on Table 2 of King. Applicants respectfully disagree. Specifically, Applicants believe that the King chapter provides an “obvious to try” rationale, rather than the requisite motivation to combine. Moreover, the King article provides a **rational approach**, which is different from the legal standard of obviousness.

Applicants specifically point to the following quotations from King, which show the unpredictability of bioisosteric replacement. King, page 207, second full paragraph explains that bioisosterism can produce “significant changes in selectivity, toxicity, and metabolic stability....” King goes on to state,

When considering any approach to lead optimization, alteration of one part of the molecule almost always affects more than just one property. Isosteric and bioisosteric replacements are no exception and this should always be considered when analyzing the result of such replacements. For example, a simple CH₂ to O to S series of replacements can alter size, shape, electronic distribution, water or lipid solubility, pK_a, metabolism, or hydrogen bonding capacity, **all with unpredictable effects upon biological activity.**”

King, page 209, first full paragraph (emphasis added). Thus, while it may be rational for one skilled in the art to try replacing a carbonyl linker with a thionyl or sulfonyl, the effect on biological activity would be unpredictable. While the King reference discusses bioisosteres, it also points out that even among bioisosteres there is really no reasonable expectation that bioisosteric replacements will yield compounds that maintain the same biological activity. Accordingly, Applicants respectfully submit that claim 1 is non-obvious over Chiesi in view of King.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 20 is rejected under 35 U.S.C. § 112, first paragraph. The Examiner first noted that the treatment of cancer is highly unpredictable, and the specification provides a description of the efficacy of the compounds in breast cancer cell lines, but because of the unpredictable

nature of cancer treatment, found that claim 20 was not enabled for all of the cancers in the claim. The Examiner noted that the only cancer lines that the claimed compounds were tested on were breast cancer cell lines.

Applicants submit that claim 20 is enabled and meets the written description requirement. While Applicants have only presented data derived from breast cancer cell lines, claim 20 and paragraph 25 of the specification lists other cancers that Applicants believe the claimed compounds will be useful to treat. Claim 20 is not so broad as to encompass all cancers. While some experimentation may be necessary to determine exact dosages, it would not be undue experimentation, but rather experimentation that is routine to one skilled in the art. Paragraphs 26-28 and 33-42 of the specification provide additional guidance to those skilled in the art. Applicants respectfully submit that claim 20, as amended, is in condition for allowance.

If issues relating to this application can be resolved by discussion, the Examiner is invited to contact the undersigned attorney by telephone. Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

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